NOT FOR PUBLICATION

UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY

SCHERING CORPORATION, Plaintiff, v. APOTEX INC. and APOTEX CORP., Defendants.	Civil Action No.: 09-6373 (PGS) REDACTED OPINION

SHERIDAN, U.S.D.J.

This is an action for patent infringement and invalidity. The Court has jurisdiction pursuant to Title 35 of the U.S. Code. More specifically, Plaintiff Schering Corporation ("Schering") alleges infringement of claims 1 and 11 of U.S. Patent No. 6,127,353 ('353 patent) on the product known as Nasonex® as well as inducement to infringe, by Defendant, Apotex, Inc. ("Apotex"). Apotex counterclaims that the '353 patent is invalid because it was obvious and anticipated. *See KSR Int'l Co. v. Teleflex, Inc.*, 550 U.S. 398 (2007).

For purposes of organization, the decision is split into two major parts (Infringement and Invalidity) and each part has a number of sections. Within Part One (Infringement), the sections are (1) the parties, (2) the patent, (3) the issues, (4) the burden of proof,(5) evidence and analysis of the facts (which is further divided into subsections named (a) testing procedures; (b) XRPD analysis and; (c) other factors) and (6) conclusion. In Part Two (Invalidity), the sections are (1) the patent history, (2) the burden of proof, (3) anticipation, and (4) obviousness.

PART ONE – INFRINGEMENT

Section 1. The Parties

Plaintiff Schering Corporation is organized under the laws of New Jersey, with its principal place of business located in Kenilworth, New Jersey. Schering is a wholly-owned subsidiary of Merck & Co., Inc. Defendant Apotex, Inc. is a corporation, incorporated under the laws of Canada, with its principal place of business located in Toronto, Ontario, Canada. It has a subsidiary, Apotex Corp., located in Weston, Florida.

Apotex filed an abbreviated new drug application ("ANDA") to produce a nasal spray to reduce seasonal and perennial rhinitis symptoms in adults and children over 12 years of age. More specifically, on or before November 6, 2009, Apotex assembled and filed (ANDA No. 91-161) with the United States Food and Drug Administration ("FDA") for generic mometasone furoate anhydrate (non-water) nasal spray, 50 mcg. [SF ¶ 5]. *See* 21 U.S.C. § 355(j)(2).

As referred to above, Schering claims Apotex's ANDA product is infringing on its '353 patent. Schering sells Nasonex® as a metered-dose, manual pump spray unit containing an aqueous suspension of mometasone furoate monohydrate (water) equivalent to 0.05% mometasone furoate calculated on the anhydrous basis (non-water).

Apotex claims its ANDA Product is different from Nasonex® because it intends to manufacture a nasal spray which contains mometasone furoate anhydrous (non-water). As such, Apotex alleges that its active pharmaceutical ingredient ("API") is different—anhydrous as opposed to monohydrate.

Section 2. The Patent

The '353 patent was issued from U.S. Patent Application No. 07/984,573 ("the '573

application") on October 3, 2000.[1] The '353 patent is directed towards a composition of matter and focuses the novel crystalline form of mometasone furoate; as well as on various types of pharmaceutical compositions utilizing mometasone furoate monohydrate. (T. 1291, 22). Schering claims Apotex infringes upon Claims 1 and 11 of the '353 patent. Claim 1 of the '353 patent describes the compound 9α,21-dichloro-16α-methyl-1,4-pregnadiene-11β ,17α-diol-3,20 dione-17-(2-furoate) monohydrate, which is also referred to as mometasone furoate monohydrate. Claim 5 of the '353 patent is directed to the compound 9α,21-dichloro-16α-methyl-1,4-pregnadiene-11β,17α-diol-3,20-dione-17-(2' furoate) monohydrate as exhibiting x-ray crystallographic powder diffraction pattern (XRPD) having certain peaks with particular spacing and intensity.

Claim 6 is directed to a pharmaceutical composition comprising mometasone furoate monohydrate in a carrier consisting essentially of water. Claim 11 is dependent on Claim 6 and is directed to the pharmaceutical composition of Claim 6 formulated as a nasal spray. Claim 11 of the '353 patent specifically claims the use of mometasone furoate monohydrate in a nasal spray formulation.

In addition to the above, the '353 patent discloses several different testing methods to determine whether a compound or formulation contains mometasone furoate monohydrate. Among these methods are water analysis, x-ray particle diffraction ("XRPD"), and infrared spectroscopy. ('353 patent, col. 1, ll. 50-67).

The '353 patent provides a graph (figure 1) showing the infrared spectrum of crystalline mometasone furoate monohydrate and a graph of the XRPD of crystalline mometasone furoate

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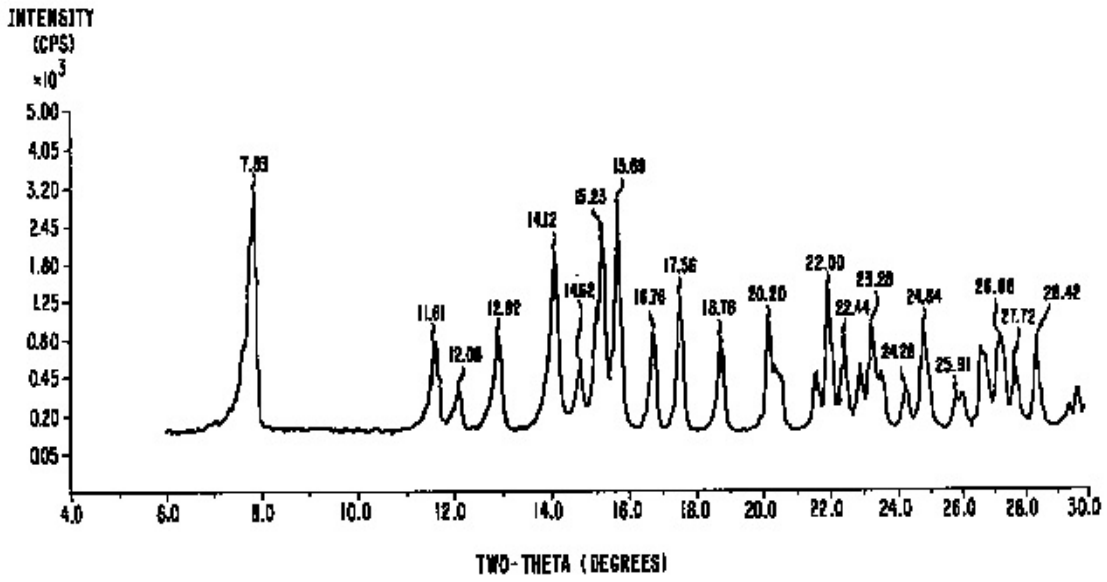
[1] As noted previously, the prosecution history is set forth in Part II, *infra*.

monohydrate (figure 2). (PTX-2 at figs. 1 and 2).

Based on the '353 patent data, if the monohydrate form existed in the Apotex ANDA Product, the results of an XRPD analysis on the Apotex ANDA Product should closely correspond to the graph in figure 2 of the '353 patent. That is, the Apotex ANDA Product exhibited through XRPD testing should be analyzed to determine whether it has certain peaks with particular spacing and intensity as detailed in the '353 patent. Figure 2 of the '353 patent is as follows:



Section 3. The Issues

Since the '353 patent sets forth a graph which depicts a monohydrate, the proof, at first glance, would be to compare the XRPD graph in figure 2 to of the monohydrate to the XRPD results of a sample of the Apotex ANDA Product. If there is a match, then infringement occurred. Unfortunately, the proofs are not so simple for several reasons.

First, there is no allegation by Schering that Apotex used a monohydrate at the time of manufacture. Schering's claim is that the anhydrate in the Apotex ANDA Product converts to a monohydrate between the date of manufacture and its expiration date (two years). Hence, to prove infringement, Schering must show that conversion occurred within two years after manufacture (the "Time Period").

Second, the mometasone furoate monohydrate depicted on figure 2 of the '353 patent was very pure, while the Apotex ANDA Product surrounds the mometasone furoate with several materials such as Avicel which is a "sticky" substance. Hence, in order to have a more sensitive depiction of the mometasone furoate during XRPD testing, Schering needed to remove the other ingredients prior to testing. This was accomplished by shaking or heating the Apotex ANDA Product. These methods used to remove the other ingredients prior to XRPD testing gave rise to the issue of whether Schering's expert fundamentally changed the substance of the Apotex ANDA Product.

The last issue concerns whether the XRPD testing results as shown in figure 2 of the '353 patent must be matched in whole or in part to conclude that the anhydrate converted to a monohydrate.

Section 4. The Burden of Proof – Preponderance of the Evidence

Generally, in a non-jury case such as this, the Court must determine whether Schering met its burden of proof. In this case, the standard is by a preponderance of the evidence. The model jury instructions give a framework that the Court can use to guide its decision here. Paraphrasing the model charge, Schering has to prove, in light of all the evidence, that what it claims is more likely so than not so. To say it differently; if you were to put the evidence favorable to Schering, and the

evidence favorable to Apotex on opposite sides of the scale, Schering would have to make the scales tip somewhat on its side. If Schering fails to meet this burden, the verdict must be for Apotex. If one finds after considering all the evidence that a claim or fact is more likely so than not so, then the claim or fact has been proven by a preponderance of the evidence. *See Model Jury Charges §1.10, Preliminary Instructions, Preponderance of the Evidence.*

In determining whether the facts have been proven by a preponderance of evidence in this case, the Court must consider the testimony of all witnesses, regardless of whom may have called them, and all exhibits received in evidence, regardless of whom may have produced them. This "standard required an analysis and weighing of all the evidence presented on both sides." *See United States v. Montague*, 40 F. 3d 1251, 1254-55 (D.C. Cir. 1994).

Section 5. Evidence and Analysis of Facts

A. Testing Procedures

Schering retained Dr. Adam Matzger[2] to analyze the Apotex ANDA Product to determine whether it converted from an anhydrate to a monohydrate within the Time Period. Apotex produced 41 bottles of its ANDA Product for Dr. Matzger to test. However, testing on the Apotex ANDA Product did not occur until the samples were near or beyond the Time Period. That is, the contents of the Apotex ANDA Product were manufactured in June 2008 and the testing occurred in

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[2] Adam Matzger is currently a Professor of Chemistry and of Macromolecular Science and Engineering at the University of Michigan in Ann Arbor, MI. He is also Co-Founder, President, and CEO of ChemXLerate, LLC, which provides analytical services, including solid state characterization of materials and chemical characterization. Dr. Matzger's expertise focuses on organic materials in the solid state with a particular interest in the crystallization of pharmaceutical compounds and related molecules. He received his Ph.D in Organic Chemistry from the University of California at Berkeley in 1997, and has a B.A. in Chemistry from Oberlin College in Oberlin, OH in 1992.

September 2010—more than two years after the manufacture date. Hence, it was critical for Dr. Matzger to resolve how he would prepare the Apotex ANDA Product to show conversion within the Time Period.

When Dr. Matzger first received the Apotex ANDA Product samples, he did not perform any XRPD tests on the samples to see if the monohydrate appeared.[3] Dr. Matzger thought that in order to investigate the contents of the Apotex ANDA Product, he must first understand the contents of the product, and then generally adjust his methodology to obtain the most sensitive results from an XRPD analysis.

The Apotex ANDA Product formulation is as follows:

[Formulation Redacted]

Dr. Matzger testified that he prepared samples of the Apotex ANDA Product to accelerate conversion from an anhydrate to a monohydrate in order to determine if the conversion occurred within the Time Period. Dr. Matzger labeled each bottle and then he subdivided bottles into numerous samples which were placed in glass vials. (T. 259, 2-5). About sixty samples were prepared.

According to Dr. Matzger, the ingredient most difficult to eradicate or separate from others to determine whether monohydrate was present is Avicel. The Avicel ingredient is "sticky," (T. 299, 3), or like the molecules are sitting inside glue, (T. 160, 22), and in order to achieve greater sensitivity in the XRPD analysis, the Avicel must be separated from the rest of the sample. In

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[3] Such XRPD analysis may have shown that several months after the expiration date, the Apotex ANDA Product converted to the monohydrate. If this occurred, it would most likely be circumstantial evidence that the conversion occurred and somehow linked backward.

addition, the concentration of mometasone furoate within the Apotex ANDA Product would be something less than one-part-in-2000, (T. 252, 4-5), and as such, Dr. Matzger recognized that the samples must be prepared to achieve high levels of sensitivity. (T. 261, 1-10) (T. 270, 6-23) (T. 296, 17 through T. 297, 9). Hence, Dr. Matzger centrifuged some samples (1-to-3 times), and he also shook (T. 208, 18), rotated (T. 210, 4-8) and spun (T. 208, 18-23) some samples. Other samples were simply centrifuged 3 times (APOMOM 12242, 12245, 12246 and 12247). Dr. Matzger found these procedures to be relatively standard techniques within his field[4]. (T. 252, 9).

Dr. Threlfall,[5] an expert for Apotex, was critical of the tests performed by Dr. Matzger. (T. 868, 24 through T. 869, 2). Dr. Threlfall noted that other ingredients in the Apotex ANDA Product were "thickening agents, preservatives, or protective colloids, such as pH controlling reagents," (T. 871, 7-10), and as such, every cell is particularly important. For instance, Dr. Threlfall indicates that a thickening agent coats both the molecules and the crystals (protective colloid) and hinders agglomeration; the buffers control the pH of the solution to prevent API from becoming to acid; and the benzyl conium chloride acts as an anti-coagulate upon the molecules and crystals. (T. 871, 15-22). Further, Dr. Threlfall indicated that only 25 of the 60 samples tested by Dr. Matzger "were claimed to have monohydrate," and he disagrees whether any of them showed monohydrate.

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[4] Annexed is a chart showing the tests performed by Dr. Matzger.

[5] Terence L. Threlfall is presently a Senior Research Fellow in the Department of Chemistry at the University of Southampton, United Kingdom. Dr. Threlfall's area of expertise is polymorphism and other aspects of solid state crystal structure and behavior, and in understanding crystallization and transformation processes. Additionally, Dr. Threlfall's research interests are in relating molecular structure to crystal structure using structural systematics and in applying spectroscopy and microscopy to crystallization and to solid-solid transition processes. Dr. Threlfall received a B.S. in Chemistry from London University in 1956, a Ph.D. in Organic Chemistry from London University in 1971, and a L.L.B. from the University of London in 1984.

Dr. Threlfall found Dr. Matzger's testimony troubling in four ways. Dr. Threlfall stated:

> I think he went wrong at four levels: I don't think he applied proper scientific judgment to his testing; I think that the design of his experiments was wrong; the actual performance of experiments leads a lot to be desired; and I think that he analyzed the data incorrectly.

(T. 909, 15-19).

Dr. Threlfall opined that Dr. Matzger had "the mindset of an advocate rather than of a scientist. And in particular, Dr. Matzger went on the hunt for traces of material, without really applying scientific judgment, ..." (T. 910, 10-14). Although Dr. Matzger found that conversion begins to occur as soon as the Apotex ANDA Product is manufactured, Dr. Threlfall's calculation was far different. According to Dr. Threlfall, the "Apotex formulation would be stable against conversion to the monohydrate for around 800 years." (T. 922, 21-24).

Dr. Threlfall was very critical of the shaking or vortexing procedure of Dr. Matzger. Dr. Matzger indicates that the shaking was "gentle." Dr. Threlfall disagreed, he honed in on vortexing.

> A. Vortexing is an even more energetic process. I mean it's like creating a mini tornado within the tube. And you can imagine that sort of -- smashes all things to pieces, it grinds the nuclei together, it causes them to break and nascent surfaces to form, and nascent surfaces are much more susceptible to change than the intact one would be, because they lost their coatings basically for a moment, and therefore they can change when they wouldn't have otherwise been subjected to change.

(T. 925, 18 through T. 926, 1). Likewise, Threlfall was critical of the washing. He opined that Dr. Matzger "washed out some of the essential components," (T. 926, 8-10), and that the removal of Avicel by shaking and washing was deleting its "protective coating." (T. 926, 20). Threlfall likened the removal of Avicel to an explorer sent to the Arctic, and then his clothes are "pinched, and you leave him in his underwear." (T. 926, 19-23). Evidently, Threlfall believes that when Dr. Matzger

washed and shaked the Apotex product, he was undermining the stability of the compound. (T. 926, 23-24).

In commenting on Dr. Matzger's procedures, Threlfall stated "I would describe this as making scrambled eggs and then claiming you still had the eggs with the shells in the carton." (T. 927, 17-19).

The issue is whether Schering met its burden of proof by a preponderance of the evidence with regard to the existence of monohydrate when the samples were shaken or vortexed to the extent that the material may have changed. Dr. Threlfall opined that Avicel "gels around the material . . . [and] in human terms [its] like swimming through molasses.' (T. 920, 6-9). Avicel is thixotropic, which means "not only does it thin when you shake it . . . but it continues to thin with more shaking." (T. 921, 12-15). Accordingly, as shaken, "Avicel reduces its viscosity by a factor of 10,000." (T. 921, 21-22).

Although Dr. Threlfall may have exaggerated some of his opinions through his colorful analogies, his demeanor was truthful. Dr. Threlfall connoted that Dr. Matzger overstepped the boundaries of a disciplined scientist. The Court gives weight to Dr. Threlfall's testimony. With regard to the samples that were shaken or vortexed, Schering has not met its burden of proof by a preponderance of the evidence. If one places the evidence favorable to Schering on one side of a scale, and all the evidence favorable to Apotex on the other, the scale does not tilt toward Schering. As such, Schering can not meet its burden of proof on any samples that were shaken or vortexed.

B. XRPD Analysis

Putting aside the samples that were shaken, there are at least four samples which were only centrifuged. The samples were marked as APOMOM 012242, 012245, 012246, and 012247. (T.

270, 6-23) (PTX-193 at 18-23). In order to increase sensitivity of the XRPD test for the Apotex's ANDA Product, it was necessary to reduce it to a solid through centrifugation. Dr. Matzger prepared the samples (APOMOM 012242, 012245, 012246, and 012247) as follows. Each sample was prepared "to get a better signal to noise for the samples." Dr. Matzger centrifuged the material three times, "trying to separate the crystalline material out in particular to gain better signal to noise." (T. 270, 19-22). In between the centrifuging, each sample was mixed slightly "to help remove the water soluble components" from the formulation, (T. 270, 23 through T. 271, 2), and water was added twice. After the last centrifugation, "the water that was used as washes . . . was decanted and the solid material at the bottom was loaded for analysis into the x-ray diffraction cell . . ." (T. 271, 5-12).

Similarly Dr. Butcher[6], an expert for Apotex, conducted XRPD tests of certain samples. Dr. Butcher undertook a similar process. Dr. Butcher centrifuged each sample four times. (T. 719, 9). After the first centrifuge he decanted the sample and replaced it with an equal volume of distilled water. (T. 718, 19-22). Hence, the centrifugation and washing of the samples is consistent for both Apotex and Schering. As such, these samples are different from the major criticism of Dr. Threlfall as set forth in the last section. In addition, Dr. Cockcroft acknowledged that he was "happy" with the centrifugation step. (T. 827, 3-4).

Since XRPD results are a critical part of the analysis for issuance of the '353 patent, such

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[6] Raymond Butcher is currently a Professor in the Department of Chemistry at Howard University since 1997. Dr. Butcher has published over eight hundred publications including articles published in journals such as *Structural Chemistry*, *CrystEngComm*, *Organic & Biomolecular Chemistry*, *Journal of the American Chemical Society*, and *Angewandte Chemie*. Dr. Butcher received a B.Sc. with Honours in Chemistry from the University of Canterbury, New Zealand in 1968, and a Ph.D. in Inorganic Chemistry and X-Ray Crystallography from the University of Canterbury, New Zealand in 1974.

testing was conducted to determine if a monohydrate could be found in the Apotex ANDA Product. More specifically, Schering claims that the anhydrate converts to a monohydrate prior to its expiration of two years from manufacture date (Time Period) and as such infringes on the '353 patent. The primary issue at trial was whether the conversion occurred.

XRPD is the standard method for looking at solid materials and polymorphs. (T. 228, 17-23).[7] XRPD looks at arrangement and characteristic spacings of molecules by measuring the intensity of refracted X-rays at different angles. (T. 230, 10-20). According to Dr. Matzger, XRPD is relatively sensitive and excellent at being able to differentiate between different forms of the same compounds. (T. 228, 17-23). Dr. Cockcroft found that Dr. Matzger did not find peaks due to the lack of intensity; and at best, he found "bumps." (T. 781, 13).

Dr. Cockcroft,[8] an expert for Apotex, noted that x-ray diffraction is covered by a very simple equation "developed by Nobel prize winner William Brack in 1913." The Brack formula relates "to the two-theta values in a diffraction powder" in terms of intensity. (T. 780, 13-21). Based on this formula, the XRPD testing device (diffractometer) was created, and it depicts material on a graph based on the intensity of its peaks. In Dr. Matzger's testing, he used an automatic diffractometer on

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[7] XRPD and PXRD are the same test for x-ray powder diffraction. (T. 227, 18) (T. 838, 4 through T. 839, 3).

[8] Jeremy Karl Cockcroft is presently a Senior Lecturer in the Department of Chemistry, University College London, United Kingdom. Dr. Cockcroft's expertise is in powder x-ray diffraction ("XRPD"). Specifically, Dr. Cockcroft's research has ranged from XRPD instrumentation to the development of software for the characterization of compounds using the technique. Recently, he established a new XRPD laboratory specialized in evaluating how temperature differences impact upon the solid state forms of a wide range of samples from ceramics to pharmaceuticals. Dr. Cockcroft received a B.A. in Chemistry from St. Catherine's College, Oxford in 1981, and a Ph.D in Chemistry from Oxford University in 1985.

which he set the scan through the two-theta angles. Once he filled a cell with the prepared sample, the diffractometer then automatically records any peaks based on the intensity on a graph. (T. 262, 21-25). A peak is produced by a clear signal or intensity. That is, the diffractometer "measures an intensity at each angle . . . so [there] is an intensity versus two-theta peak." (T. 261, 3-6). Often the prepared sample may have some different materials commingled in it during XRPD testing, and the peak may be surrounded by noise (non-peak sound). The signal to noise factor was critical in this case for several reasons.

First, according to Dr. Matzger there were significant overlaps between peaks of mometasone furoate anhydrous and mometasone furoate monohydrate at 20 values above approximately 12 degrees. As a result, it would have been impractical for Dr. Matzger to collect or analyze data from higher 20 values (T. 437, 16 through T. 438, 19), and accordingly, Dr. Matzger limited his findings to those under the 20 values. Hence, Dr. Matzger analyzed only a portion of the peaks shown on figure 2. of the '353 patent.

Second, the monohydrate depicted in figure 2 was very pure, while the materials in the prepared sample were commingled with other materials that were not separated, and this may have created noise during Dr. Matzger's testing. In order to determine whether a peak exists, it must rise significantly above the noise levels in the diffractional data. (T. 781, 11-15).

Third, the signals from the XRPD conducted by Dr. Matzger must relate to the peaks of figure 2. The issue which arises is how many peaks on figure 2 can be matched to the prepared sample to show a monohydrate. Dr. Matzger indicates that it should be a subset of the peaks in figure 2. (T. 620, 8-15). Dr. Matzger found that a match showing a monohydrate existed if 1 or 2 peaks were shown. Dr. Cockcroft indicates that at least three peaks must be shown to identify a

monohydrate based on practice in the field. That is, it is "accepted practice to use at least three peaks, often more to identify material." (T. 779, 23-24). Dr. Cockcroft noted that crystals are three dimensional objects, and to measure these crystals, one must find length, width and depth, and each peak must be unique. If two peaks are the same, or a factor of each other, it could be a duplication. (T. 785, 1-7) (see below).

According to Dr. Cockcroft, the history of the three peaks standard is derived from the work of Mr. Hanawalt. Evidently, in the 1940's, Hanawalt was researching numerous minerals which required him to perform XRPD tests on many minerals. Since there were so many samples, Hanawalt devised a database of XRPD patterns so he could identify each one. In developing a card system to identify each sample, he listed the three most intense peaks of the material on a separate card. This format became known as the Hanawalt Search Index. (T. 788, 4-12). Due to this practice, most scientists still use three peaks to identify a pattern. (T. 788, 4-12).

Lastly, the use of the Brack Formula recognizes that if a peak occurs at a specific level (say 7.8 degrees) and another peak occurs at a factor of 2 (say 15.6), the second peak is a duplication of the first; and hence it is not considered a unique peak (T. 780, 19-25). Hence, duplication must be considered in analyzing XRPD results.

All four samples were subject to XRPD analysis and recorded on a graph (PTX-451). In each of the samples, Dr. Matzger found "evidence of conversion" with peaks at 7.8 and 11.6 as recorded on figure 2 of the patent. (T. 272, 19-25).[9] On sample 012245, Dr. Matzger found that XRPD showed three peaks "consistent with conversion," namely 7.8, 15.6 and 11.6. (T. 277, 13-19). With

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[9] PTX-479 was also admitted because it is another chart about APX 102242 with different scaling. (T. 275, 7-16).

regard to the 15.6 peak, it is a factor of 2 of the 7.8 peak. Dr. Matzger noted it "illustrates . . . the problems you can have with overlap because there is a shoulder here that is associated with the 15.6 degree peak as opposed to a "distinct peak as it did in the previous pattern." (T. 278, 11-18) (PTX-480). Despite the fact that it is a shoulder and not a peak, he opined that "its all consistent with conversion." (T. 278, 20). In sample 012245, Dr. Matzger fails to consider the limitation within Brack's formula (see above). Dr. Cockcroft had indicated that a peak at 7.8 and a peak at 15.6 were duplicative based on the application of the Brack formula. Hence, in sample 012245, there are not three peaks as Dr. Matzger finds, but only two in accordance with the Brack formula. Dr. Matzger never refuted the Brack formula, as such, the limitations within the Brack formula are credible.

In reviewing samples 012242, 012246, 012246 and 012245, there are only two peaks shown. The testimony of Dr. Cockcroft about the need to find three peaks seems more reasonable than Dr. Matzger's "subset" analysis. Figure 2 of the '353 patent disclosed a graph with at least 25 peaks showing the monohydrate. To rely on one or two peaks is insufficient upon which to find a match to figure 2. As such, Schering failed to meet its burden of proof that a monohydrate existed in the Apotex ANDA Product based upon the XRPD analysis considered.

C. Other Factors

Dr. Matzger opined that his XRPD tests should control because his results make sense in light of three other items—preferred orientation, the Bodycote Report, and Raman Spectrography. Each is discussed below.

(a) Preferred Orientation

Preferred orientation is a concept which explains why certain peaks can not be found on the XRPD results. By example, Dr. Matzger stated rain that freezes is "spherical, hail shaped, there's

no real orientation . . . they come down at random." Opposed to that are "a bunch of pennies" that fall on a table, they will adopt one orientation" that is flat. (T. 233, 1-10). This happens in pharmaceuticals when different shapes of crystals may "lead to a different arrangement" (T. 233, 12-14). Due to preferred orientation if all the crystals are laying flat, "not all of the peaks will be observable." In fact, "you can have cases where preferred orientation is extreme enough that peaks are not observed." (T. 234, 17-18).

Dr. Cockcroft disagrees. Dr. Cockcroft indicated if pennies were thrown on a table, "some lie flat compared to some lying randomly, tilted on angels. And that's what meant by preferred orientation, that there is a preferential direction with regard to the crystallites." (T. 822, 18-25). Dr. Cockcroft was incredulous about Dr. Matzger's finding. He stated:

> Because the theory that he's advocating is one so extreme that he's simply saying all the other peaks vanish. And as I just explained to your Honor, you can have degrees of preferred orientation, you may expect the majority of say the coins to lie one way up; you don't expect a hundred percent of them to lie one way up. And therefore you still expect to see, maybe with lower intensity, the other peaks in the powder x-ray diffraction pattern.

(T. 825, 12-19).

Dr. Threlfall also disagreed with Dr. Matzger's findings on preferred orientation. Dr. Threlfall stated Dr. Matzger "ignored" some data. He stated:

> A. Well, in his preferred orientation theory he suggests that he didn't see the 14.1, 15.2, and indeed also the 17.5, the 18.7; and in one case even as he actually went as far as 34 degrees two-theta, the 31.2 degrees peak, which is actually a substantial -- surprisingly substantial peak in the reference monohydrate, which is actually the third order of the 7.8 peak. So he should have observed that even in preferred orientation circumstances, but he just ignored that. Ignored all the things that he didn't want to see.

(T. 910, 19 through T. 911, 2). In the Court's view, the practice of finding three peaks as per the Hanawalt practice is very sound. The preferred orientation explanation tends to undermine the practice of finding three peaks, and applying preferred orientation to all prepared samples appears to be overly aggressive in light of Dr. Cockcroft and Dr. Threlfall's testimony. Little weight is given to the preferred orientation theory.

(b) Bodycote Report

Dr. Matzger argues that his findings are consistent with the conclusions of the Bodycote Report, and therefore his findings should be considered reasonable. By way of background, in 2000, Bodycote Ortech authored a report confirming that the anhydrate converted to monohydrate (T. 304, 19-22). Dr. Hui, a product manager at Novex, testified that in 2000 Bodycote had tested mometasone furoate on behalf of Novex Pharma, a close affiliate of Apotex. Dr. Matzger focused on the XRPD results of three different formulations of Bodycote testing. Within the Bodycote Report, Dr. Matzger stated there were findings that "there was conversion in the formulations . . . of anhydrous mometasone furoate anhydrate to . . . a monohydrate." (T. 310, 1-4). More particularly, Dr. Matzger focused on three formulations (4A, 4B and 4C) that were subject to XRPD testing within seven weeks after production. Dr. Matzger was most impressed with the XRPD results of formulation 4A because it is "the closest to Apotex's ANDA Product." (T. 328, 1-5). The "two most important things" from the formula 4A results were "one is it shows the 7.8 degree peak . . . consistent with conversion to a mometasone furoate monohydrate [and] that's also the only prominent peak difference between that and anhydrous mometasone furoate. And so it shows that you can get strong preferred orientation in this system." (T. 330, 4-10).

In addition to Dr. Matzger's comments, Dr. Kovacs, an Apotex representative, testified at his deposition that the Bodycote Report found that seven weeks after production of formula 4A, it contained both monohydrate and anhydrate forms. (Kovacs Depo. at T. 175, 2-10).

Apotex denies that formula 4A contains monohydrate. Apotex argues that the Bodycote Report is over ten years old and therefore remote. In addition, it is likely to be either (1) "a degradation product; or (2) the 2.5% crystal identified by Dr. Eckhart (T. 123, 19 through T. 124, 3); or (3) it lacks sufficient peaks on the XRPD test to be considered a monohydrate.

The Court finds that the Bodycote Report is relevant; but the Report itself was not supported by any first hand testimony or evidence by a person performing or overseeing the test. Although it may support Dr. Matzger, it does not add much weight to his testimony in light of Dr. Cockcroft's and Dr. Threlfall's testimony.

(c) Raman Spectroscopy

Raman Spectroscopy provides information about the vibrational modes of bonds in a molecule. (T. 229, 11-21). Dr. Matzger noted the difference between Raman and XRPD testing, "with the x-ray you analyze the whole sample at once, and because this [Raman] is hooked up to a microscope we can look at it piece by piece and actually figure out where . . . different particles, what form they are [and] if we're looking at, for example, mometasone furoate or other places in the system." (T. 229, 4-9). Since Raman gives information about vibrational modes in a molecule, you learn "literally the way the atoms are vibrating within a molecule, which is a characteristic." (T. 229, 11-14). In the '353 patent, Raman Spectroscopy is not named as a testing method, but infrared spectroscopy is so named. Dr. Matzger explained that infrared and Raman are related as a "slightly different flavor of vibrational spectroscopy." (T. 229, 14-20). More particularly, Raman provides

more information about spatial distribution and due to the smallness of particle size of the monohydrate Raman provided "superior" resolution. (T. 624, 14-19). Dr. Matzger concluded that both the XRPD and the Raman testing "showed substantial conversion in" samples 012242, '45, '46 and '47 as well as sample 012225. (T. 405, 23 through T. 406, 15). To the contrary, Dr. Cockcroft and Dr. Threlfall found the same problem as they did with Dr. Matzger's XRPD findings—there were less than three peaks found, and therefore a monohydrate cannot be identified as a result of the Raman testing. (T. 943, 7-13).

Dr. Matzger's Raman findings are at odds with the results of Raman tests completed by Dr. Spingarn[10] on behalf of Apotex. Dr. Spingarn performed Raman testing on ten random particles of the Apotex ANDA Product. He sprayed a sample onto a filter and let the liquid drain out. (T. 654, 1-3). From the solids on the filter, he focused on the "smaller particles" that were crystalline and had sharp edges. (T. 651, 20-23). From his Raman testing he found there "was no evidence of . . . [a] monohydrate in the sample," and the crystals were relatively uniform in size and appearance." (T. 656, 11-15).

The Court finds that the Raman Spectroscopy as relied upon by Dr. Matzger has little weight because it does not identify three peaks, and there is a significant difference in test results between Dr. Spingarn and Dr. Matzger.

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[10] Neil Elliot Spingarn is the President of S & N Laboratories, an independent testing laboratory located in Santa Ana, California since 1984. Dr. Spingarn's expertise is in all aspects of microanalysis, and in particular conducting Raman Spectroscopy measurements. Dr. Spingarn received a B.A. in Biochemistry from the University of California at Berkeley in 1974, a M.S. and M. Phil. in Pharmacology from Yale University in 1976, and a Ph.D. in Pharmacology from Yale University in 1978.

Section 6. Conclusion

Based upon the facts and conclusions reached above, the Court finds the complaint based upon infringement is dismissed because Schering has failed to present credible evidence sufficient to meet its burden of proof by a preponderance of the evidence standard.

PART TWO – INVALIDITY

Section 1. The Patent History

In the early 1980's, Elliot Shapiro, a chemist employed by Schering, first synthesized anhydrous mometasone furoate. (FPTO at 7). On July 29, 1982, Schering filed an application for a patent on anhydrous mometasone furoate, and the Patent No. 4,472,393 was issued on Sept. 18, 1984 (the "Shapiro" patent). After its discovery, mometasone furoate anhydrate was placed on Schering's "backburner" because of very unique physical properties which created a hurdle for development. Among these properties was the fact that mometasone furoate anhydrate was an insoluble compound in water, and known pharmaceutically acceptable solvents were unable to dissolve the compound. (Sequiera Depo. at T. 65, 2 through T. 66, 19).

In the early to mid-1980's, researchers at Schering discovered that mometasone furoate could be dissolved with one of the newer pharmaceutical solvents, hexylene glycol. (Sequiera Depo. at T. 66, 20 through T. 67, 2). After discovering that mometasone furoate could be dissolved with hexylene glycol, Schering pursued a mometasone furoate formulation for the treatment of psoriasis, a skin condition. (Sequiera Depo. at T. 77, 7-25).

Until the discovery of mometasone furoate monohydrate reflected in the '353 patent, the only known form of mometasone furoate was the anhydrous form. (PTX-2 at 1:18-28). Subsequently, in the late 1980's, Schering began considering other, nondermatological uses for mometasone furoate anhydrous. (T. 60, 4-22) (T. 67, 18-23), and at that time, Dr. Pui-Ho Yuen, a formulator at Schering,[11] took responsibility for a project to develop mometasone furoate into nasal applications.

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[11] While at Schering, Dr. Yuen held the positions of Senior Scientist, Associate Principal Scientist, Principal Scientist, and Senior Principal Scientist. (T. 31, 2-11). He is co-inventor of the

(T. 31, 22-25). It took about 2.5 years to develop the alleged invention. There were many trials and errors. In order to develop the alleged invention, Dr. Yuen researched the literature to determine how to formulate a suspension for nasal delivery, and gathered information that Schering had gathered on mometasone furoate. His initial research on the background showed that there was very little information regarding aqueous nasal suspension formulations. (T. 36, 5-8).

Dr. Yuen uncovered that nasal sprays can be formulated as both suspensions and solutions. In 1988, only two glucocorticosteroids were approved for intranasal use in the United States—beclomethasone dipropionate and flunisolide. (T. 974, 7-12). One of these was a suspension, and one was a solution. (PTX-394 at 344). In 1987, Dr. Yuen set out to formulate a suspension[12] of mometasone furoate for nasal application. (T. 31, 22-25).

Dr. Yuen concluded that to formulate a suspension of mometasone furoate, he must consider particle size, distribution, the pH of the product, and solubility in water. (T. 34, 11-18). Dr. Yuen recognized also that the product must not cause irritation to the user. (T. 35, 17-24). The particle size of the active ingredient can affect the efficacy of the product. (T. 54, 9-22). The problem Dr. Yuen confronted was that solid particles in suspension settle. This requires a thickening or suspending agent, in order to increase the viscosity of the liquid, and slow settling. (T. 35, 9-16).

Over a period of two years, Dr. Yuen and his lab assistant, Teresa Etlinger, developed between 30 and 40 formulations. (T. 36, 9-20). The original formulas were "to assess the stability

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'353 patent.

[12] A suspension is a formulation in which the active ingredient remains in a solid state, undissolved, and is suspended in a liquid vehicle. (T. 34, 11-14).

of the suspension." (T. 38, 8 through T. 39, 14). During this time, Dr. Yuen and Ms. Etlinger noticed that some of the formulations showed particle size growth (which is not a desirable effect). (T. 39, 12-16). As a result, Dr. Yuen and Ms. Etlinger attempted to formulate different formulations to thwart the particle growth problem. That is, they changed the suspending agent and employed different preservatives and antimicrobial agents. (T. 39, 17-20). None of these solutions worked. Dr. Yuen and Ms. Etlinger regularly submitted prototype formulations for analysis. (T. 39, 17-19).

In the fall of 1988, Nancy Levine, one of the co-inventors on the '353 patent, ran tests on some of the samples. (PTX-322 at 76-77). The testing revealed that a new compound might be present in at least one of these samples. As a result, additional testing occurred. (T. 94, 12 through T. 98, 12). More specifically, Ms. Levine conducted initial stability tests, and then had the stability samples subject to X-ray powder diffraction testing. (T. 89, 25 through T. 90, 22). As noted previously, XRPD testing allows one to look at the solid state structure of a particular compound. (Eckhart Depo. at T. 27, 14 through T. 28, 4). The test results on the September 22nd sample stated that "[t]he [XRPD] and microscopic data support conversion of the original mometasone furoate crystal structure to a second, possibly solvated, form." (T. 92, 10-17).

Mr. Eckhart testified that the XRPD pattern he generated on the samples did not match up with the reference standards he had seen previously for mometasone furoate. (Eckhart Depo. at T. 108, 10-17). Mr. Eckhart conducted additional testing on other formulations of mometasone furoate nasal spray. Some, but not all, of the tests showed conversion of the anhydrous form of mometasone furoate to the second form (the monohydrate). (T. 98, 13-100). As a result, the larger sized particle that was appearing in some of the formulations was the active ingredient, mometasone furoate, in a different crystalline form. (T. 41, 4-11). According to Schering, this discovery occurred in

November of 1988. (T. 41, 12-16).

Before this discovery, it was not known that mometasone furoate had different crystal forms. (T. 41, 12-16) (T. 108, 17-20). The second form of mometasone furoate was ultimately identified as mometasone furoate monohydrate. (T. 133, 17 through T. 134, 18). The conversion of anhydrous mometasone furoate to the monohydrate form did not occur in all formulations, and appeared to be unpredictable. (T. 41, 25 through T. 42, 5).

After Dr. Yuen discovered that the anhydrous mometasone furoate converted to the monohydrate form in certain formulations, he began considering whether he could create a formulation using the monohydrate form at the outset. (T. 41, 17-24).

In the summer of 1989, Dr. Yuen formulated several new formulations using mometasone furoate monohydrate, (T. 42, 6-18), and developed the Nasonex® formula. Based on that formulation, Schering undertook the patent process.

The Patent Office denied Schering's request for a Patent at least three times over a ten year period before its acceptance. Initially, the Patent Office did not see anything new in converting an anhydrate to a monohydrate. Oversimplfying, according to the reviewer, it was just adding water.

On September 6, 1991, Schering filed foreign Patent Cooperation Treaty (PCT) Application No. PCT/US91/06249 for another protective patent "mometasone furoate monohydrate, process for making same and pharmaceutical compositions" (the "International Application"). (DTX-49 at 411). Based on the International Application, Schering filed the '573 application on March 5, 1993 as a U.S. National Phase claiming priority from the International Application. (DTX-49 at 374). Claim 1 of both applications are directed to the monohydrate form of mometasone furoate. (*Compare* DTX-48 at col. 6, ll. 31-32 *with* DTX-49 at 391) (*see also* T. 869, 10-23). In an Office Action dated

November 8, 1993, the USPTO rejected claim 1 of the '573 application as anticipated by the Shapiro patent. (DTX-49 at 429). In rejecting claim 1, the USPTO stated that the Shapiro patent discloses a process involving recrystallization of mometasone furoate crystals from methanol:water, and that the compound produced by this process (the "Recrystallization Compound") "is inherently the monohydrate of mometasone furoate." (DTX-49 at 434-36 (citing Shapiro, col. 21, ll. 19-30)).

On March 9, 1994, Schering requested reconsideration of the '573 application. (DTX-49 at 434-36). In their request for reconsideration, Schering argued that "[t]here is no teaching, disclosure, or suggestion in the Shapiro patent itself to hydrate formation of any of the compounds claimed in the patent." (DTX-49 at 435-36). Additionally, Schering asserted that there is no evidence "to support the conclusion that mometasone furoate recrystallized from methanol: water would inherently form any hydrate molecule, much less the specific monohydrate of the subject compound." (DTX-49 at 436). In support of their arguments, Schering amended their application to include claim 7, a XRPD pattern of the claimed mometasone furoate monohydrate compound. (DTX-49 at 434, 437-38). In a Final Action dated August 1, 1994, the USPTO rejected claims 1 and 7 of the U.S. Application as anticipated by the Shapiro patent. (DTX-49 at 441). According to the USPTO,

> The mometasone furoate [in the Shapiro patent] is formed in a reaction which includes reaction in a solvent followed by the addition of 500ml of distilled water to quench the reaction. The product formed by the addition of water would be expected to be a hydrate. Additionally, absolute predictability is not required, only a reasonable expectation that the monohydrate is produced.

(DTX-49 at 441).

On December 16, 1994, Schering appealed the USPTO's July 29th decision to the Board of Patent Appeals and Interferences, but both the appeal and the application were abandoned. (DTX-49 at 445-47). On petition from Schering, the U.S. Application was eventually reopened, and on December 10, 1998, the USPTO issued a Second Non-Final Office Action, this time rejecting claims 1 through 7. (DTX-49 at 539-47). Claims 1, 2, 4, and 7 were rejected under 35 U.S.C. § 102(b) as anticipated by the Shapiro patent. In rejecting these claims, the USPTO again cited to the Recrystallization Compound, stating that it "is inherently the monohydrate of mometasone furoate." (DTX-49 at 545).[13] Claims 3, 5, and 6 were rejected under 35 U.S.C. § 103(a) as obvious under Shapiro. In rejecting these claims, the USPTO noted that these claims differed from the Shapiro patent by reciting "specific organic solvent[s]," "specific formulation," and "specific concentration of excipients," but determined that such differences were insubstantial. (DTX-49 at 547).

On March 15, 1999, Schering filed a reply to the USPTO's office action. (DTX-49 at 549-61). In an attempt to distinguish the Recrystallization Compound from the monohydrate form of mometasone furoate, Schering's reply included a declaration from Charles Eckhart, co-inventor of the'573 application. (DTX-49 at 556-61). In his declaration, Mr. Eckhart claimed that Schering re-created the Recrystallization Compound back in May 1989 as part of its efforts to develop mometasone furoate monohydrate. (DTX-49 at 557). According to Mr. Eckhart, a XRPD analysis of the Recrystallization Compound conducted on June 1, 1989 revealed only the anhydrous form of mometasone furoate. (DTX-49 at 557). In support of this claim, Mr. Eckhart attached an excerpt

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[13] The USPTO also found that the Shapiro patent "teaches [both] pharmaceutical compositions [of mometasone furoate] and the anti-inflamatory propert[ies] of [such compositions]." (DTX-49 at 545).

from the lab notebook that outlined the re-creation process and the corresponding XRPD pattern. (DTX-49 at 557-61). In a Second Final Office Action dated June 28, 1999, the USPTO rejected Schering's claims, finding that Schering's re-creation of the Shapiro patent process failed to follow the process. (DTX-49 at 562-68). According to the USPTO, the Shapiro patent calls for mometasone furoate to be mixed and dissolved in a solvent such as methanol or water. (DTX-49 at 556). The Schering re-creation of the Shapiro patent mixed and dissolved mometasone furoate in hot dicholoromethane. (DTX-49 at 556). The USPTO found this difference to be material and affirmed their earlier rejection. (DTX-49 at 556-57).

After the USPTO's Second Final Rejection, Schering reviewed the Shapiro patent files for any evidence that the Recrystallization Compound was not the monohydrate form of mometasone furoate. (DTX-49 at 570). Schering's review ultimately produced an infrared IR spectrum of the Recrystallization Compound that was generated during the development of the Shapiro patent. (DTX-49 at 571). According to Schering, the rediscovered IR (infrared) spectrum lacked prevalent water peaks. (DTX-49 at 591-99). On November 24, 1999, Schering officially replied to the Second Final Office Action, notifying the USPTO of the rediscovered IR spectrum and arguing that the absence of certain water peaks proved that the Recrystallization Compound was not a hydrate. (DTX-49 at 591-99). The USPTO found this evidence persuasive, and on December 10, 1999, the USPTO issued a Notice of Allowability. (DTX-49 at 600-02).

The '353 patent was issued from '573 application on October 3, 2000. As noted in Part I, claim 1 of the '353 patent is directed to the monohydrate form of mometasone furoate. ('353 patent, col. 6, ll. 31-32) (T. 869, 15-23). Claim 11 is directed to the pharmaceutical composition comprising mometasone furoate monohydrate in a carrier consisting essentially of water that is formulated as

a nasal spray.

On September 18, 2001, the Shapiro patent expired.

Section 2. Burden of Proof

A patent shall be presumed valid and the burden of establishing invalidity of a potent or any claim thereof shall rest on the party asserting such invalidity. *Microsoft Corp. v. i4i Ltd.*, 131 S. Ct. 2238, 2242 (2011). A party challenging the validity of any claim of a patent has the heavy burden of proving invalidity by "clear and convincing" evidence. *Id.*; *Takeda Chem. Indus. Ltd. v. Alphapharm Party Ltd.*, 492 F.3d 1350, 1355 (Fed. Cir. 2007). Clear and convincing evidence is evidence that produces in the fact finder's mind a firm belief or conviction as to the matter at issue. *See Trans World Mfg. Corp v. Al Nyman & Sons, Inc.*, 750 F.2d 1552, 1560 (Fed. Cir. 1984). The "clear and convincing" standard is an intermediate standard that lies somewhere between the "beyond a reasonable doubt" and "preponderance of the evidence" standards of proof. *Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348, 1360 n.5 (Fed. Cir. 2007). Although an exact definition is elusive, "clear and convincing evidence" has been described as evidence that "place[s] in the ultimate factfinder an abiding conviction that the truth of its factual contentions are highly probable." *Id.* (citing *Colorado v. New Mexico*, 467 U.S. 310, 316 (1984) (internal quotations omitted)).

Clear and convincing evidence is evidence that produces in your mind a firm belief or conviction that the allegations sought to be proved by the evidence are true. Clear and convincing evidence involves a higher degree of persuasion than is necessary to meet the preponderance of the evidence standard. But it does not require proof beyond a reasonable doubt, the standard applied in criminal cases.

Section 3. Anticipation

Apotex contends that claims 1 and 11 of the '353 patent are invalid under 35 U.S.C. § 102(b) for anticipation. Schering argues that anticipation was not raised previously and therefore barred under the final pretrial order. On this ground, Schering is correct. Apotex did not raise the issue of anticipation. (FPTO 362-64 (outlining Apotex's legal issues for trial)). When an issue, argument, claim or defense is not raised in the pretrial order, it is deemed waived. *Briglia v. Horizon Health Care Servs., Inc.*, 2010 WL 4226512, at *4 n.5 (D.N.J. Oct. 21, 2010) (Hillman, J.). Thus, Schering has waived this cause of action.

Additionally, the Court notes that Apotex fails to prove anticipation through clear and convincing evidence. Apotex argues that the Shapiro patent anticipates the '353 patent under 35 U.S.C. § 102(b). The statute operable statute states that "a person shall be entitled to a patent unless . . . the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of the application for patent in the United States, ..." 35 U.S.C. § 102(b). Apotex argues that recrystalizating mometasone furoate from water:alcohol mixture in the '353 patent into the monohydrate form is described in the Shapiro patent. Despite this contention, Apotex has not shown any clear and convincing evidence to rebut the following facts that: (1) the rediscovered IR spectrum delivered to the USPTO in November 1999 showed an absence of water peaks and therefore recrystallization compound was not a hydrate; and (2) the Shapiro patent does not disclose a monohydrate, hence it is not subject to 102(b) analysis. As Dr. Trout stated, "Shapiro discusses mometasone furoate, but it doesn't discuss anything about the monohydrate, or the particular crystalline form that the monohydrate would be in." (T. 1247, 14-1). Even Dr. Mitra, Apotex's expert, indicated that the

monohydrate was not disclosed. (T. 1056, 1-10). In light of same, the Court finds that Apotex did not meet its burden of proof to show anticipation by clear and convincing proof.

Section 4. Obviousness

Apotex also contends that claims 1 and 11 of the '353 patent are invalid under 35 U.S.C. § 103(a) for obviousness. A patent claim is said to be obvious if the differences between the subject matter sought to be patent and the whole of the prior art are such that the subject matter would have been obvious at the time the invention was made to a person having ordinary skill in the art. 35 U.S.C. § 103(a); *see also KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 406 (2007). A determination of obviousness is a question of law based on the facts concerning: (I) the scope and content of the prior art; (ii) the level of ordinary skill in the art; (iii) the differences between the prior art and the claims at issue; and (iv) objective indicia of nonobviousness, such as unexpected results, failure of others, long-felt need, commercial success, copying, and praise for the invention. *See Graham v. John Deere Co.*, 383 U.S. 1, 17-18 (1966); *Specialty Composites v. Cabot Corp.*, 845 F.2d 981 (Fed. Cir. 1988).

Obviousness determinations proceed in two stages. First, the patent challenger must establish by clear and convincing evidence that the claimed invention is prima facie obvious. *See Kaufman Co. v. Lantech, Inc.*, 807 F.2d 970, 974-75 (Fed. Cir. 1986). If the accused infringer fails to establish *prima facie* obviousness, the analysis is over, and the asserted claims may not be found invalid for obviousness. *Yamanouchi Pharm. Co. v. Danbury Pharmacal, Inc.*, 231 F.3d 1339, 1345 (Fed. Cir. 2000). To establish prima facie obviousness where the invention is a chemical compound, the challenger must prove, by clear and convincing evidence, two things: (1) that a person of ordinary skill would have selected a particular "known compound," and (2) there existed in the prior art a

reason to modify that lead compound "in a particular manner" so as to arrive at the compounds of the invention. *Takeda*, 492 F.3d at 1357.

(1) The level of ordinary skill in the art

The Court must determine what a person having ordinary skill in the art ("PHOSITA") would have thought at the time of the invention, guided only by the prior art and the then-accepted wisdom in the field. *In re Kotzab*, 217 F.3d 1365, 1369 (Fed. Cir. 2000). The parties agree that a PHOTISA skilled in the art pertaining to the '353 patent is a person actively involved in the drug development process. (Apotex FOF ¶ 858) (Schering FOF Reply ¶ 858). The parties further agree that the process is a multidisciplinary process that requires collaborative teamwork from persons with various experience. (Apotex FOF ¶ 859) (Schering FOF Reply ¶ 859). The parties also agree that examples of disciplines involved in the drug development process are those with backgrounds in medicine, nasal pharmacology, medicinal chemistry, physical chemistry, drug formulation, and drug delivery. (Apotex FOF ¶ 860) (Schering FOF Reply ¶ 860). The only real difference between the parties is over whether a PHOTISA would have a specific expertise in liquid dose formulations. (*Compare* Apotex FOF ¶ 861 *with* Schering FOF ¶ 861). Apotex, relying on the testimony of Dr. Mitra, claims that a PHOTISA would have such specific experience, particularly in the fields of nasal liquid dose formulations and nasal pharmacology. (T. 1022, 1-8). Conversely Schering, relying on the testimony of Dr. Trout, claims that a PHOSITA would not require specific experience in the development of aqueous nasal suspensions. (T. 1229, 1-12).

(2) The Scope and Content of the Prior Art

Apotex's position regarding the scope and content of the Shapiro patent incorporates the discussion and argument advanced in their anticipation claim—namely, that the Shapiro patent

discloses both the monohydrate form of mometasone furoate and a nasal spray developed with same. (Apotex FOF ¶¶ 809-11, 864-66). Additionally, Apotex claims that even if the Shapiro patent did not anticipate the '353 patent, a skilled pharmacologist would have been motivated to develop a nasal spray using mometasone furoate, the compound first described in the Shapiro patent. "Determining whether there is a suggestion or motivation to modify a prior art reference is one aspect of determining the scope and content of the prior art, ..." *SIBIA Neurosciences, Inc. v. Cadus Pharamceutical Corp.*, 225 F.3d 1349, 1356 (Fed Cir. 2000). A suggestion to modify or a motivation to combine prior art elements may be derived from the prior art reference itself, from knowledge of one of ordinary skill in the art, or from the nature of the problem to be solved. *Id.; see also Pro-Mold & Tool Co. v. Great Lakes Plastics, Inc.*, 75 F.3d 1568, 1573 (Fed. Cir. 1996).

In support of their obviousness argument, Apotex has identified five distinct articles of prior art: (1) the Shapiro patent; (2) J. E. Carless, at al., *Dissolution and crystal growth in aqueous suspensions of cortisone acetate*, 20 Journal of Pharmaceutical & Biomedical Analysis 630 (1968) ("the Carless Paper"); (3) U.S. Patent No. 4,414,209 filed on November 8, 1983 (the "Cook Patent"); (4) U.S. Patent No. 4,866,051 filed September 12, 1989 ("the Hunt Patent"); and (5) Chang-Jin Wang, *A competitive enzyme immunoassay for the direct determination of mometasone furoate (SCH 32088) in human plasma*, 10 Journal of Pharmaceutical & Biomedical 473 (1992) ("the Wang Paper").[14] According to Apotex, the existence and combination of these articles would have

[14] Apotex also lists Elocon® as a prior art reference. (Apotex FOF ¶¶ 194-96). Elocon® is a topical ointment based on the Shapiro patent. Since neither party identifies any material difference between Elocon® and the Shapiro patent—as least as it pertains to their existence in the prior art—the Court's discussion of whether the '353 Patent was obvious in light of the Shapiro patent incorporates all references to Elocon®.

motivated an ordinary pharmacologist as of September 6, 1990 to both choose mometasone furoate as a treatment for allergic rhinitis and to formulate mometasone furoate into an aqueous solution.

(A) Choosing mometasone furoate as a treatment for allergic rhinitis

In September 1990, skilled pharmacologists were searching for a corticosteroid that was active as an anti-inflammatory drug with minimal unwanted side effects in order to treat rhinitis. (Apotex FOF ¶ 870-72, 874) (Schering FOF Reply ¶ 870-72, 874). Apotex claims that mometasone furoate "stood out" as the most effective solution. Apotex bases their conclusion on what they claim are the two key attributes of mometasone furoate: potency and safety.

Apotex, relying on Drs. Page and Mitra, claims that mometasone furoate was known to be a potent anti-inflammatory drug. (T. 978, 19 through T. 79, 1) (T. 1028, 5-10). Drs. Page and Mitra further claim that knowledge of this potency extended to the mucous membrane, which includes the nose. (T. 979, 5-9) (T. 1028, 11-18). Dr. Page also testified that during the applicable time frame, corticosteroids were the most effective treatment of rhinitis. (T. 989, 20-22). Based on these features Dr. Page asserts that the Shapiro patent would have taught a skilled pharmacologist that mometasone furoate could be used to treat rhinitis. (T. 980, 6-16) (T. 973, 12-14) (T. 976, 3-5).

Apotex also claims that mometasone furoate was known to be safe. According to Apotex, an ordinary pharmacologist would have known that mometasone furoate was safe because as of September 6, 1990, the FDA had already approved mometasone furoate for the topical treatment of inflammatory conditions. (T. 980, 14 through T. 981, 1). Under this argument, the safety of mometasone furoate was particularly important due to the relative toxicity of corticosteroids. (Apotex FOF¶¶ 869-76 (citing T. 974, 15 through T. 975, 2)).

Apotex finds further support for their claim that mometasone furoate possessed the twin attributes of potency and safety in two articles that would have been available to an ordinary pharmacologist in September 6, 1990. The first article is Luciano Dominguez et al., *Comparison of the Safety and Efficacy of Mometasone Furoate Cream 0.1% and Clobetasone Butyrate Cream 0.05% in the Treatment of Children with a Variety of Dermatoses*, Current Therapeutic Research 128-39 (July 1990) (the "Dominguez Article"). According to Dr. Page, the Dominguez Article concluded that mometasone furoate has a significant therapeutic advantage over a number of other corticosteroid formulations, that it possesses superior efficacy even when applied once daily, and that it was safe. (T. 982, 16 through T. 983, 6; DTX-407 at 129). Additionally, the parties agree that the efficacy of once-a-day-treatments would have been important during the applicable time period given a known patient preference for once-daily treatments. (Apotex FOF ¶ 892; Schering FOF Reply ¶ 892). The second article is Renie Bressinck, M.D. et al., *Comparison of the Effect of Mometasone Furoate Ointment 0.1%, and Hydrocortisone Ointment 1%, on Adrenocortical Function in Psoriasis Patients*, Today's Therapeutic Trends 25-35 (1988) (the "Bressinck Article"). The Bressnick Article was a comparison of the effect of mometasone furoate ointment and hydrocortisone ointment, another steroid available at the time. (Apotex FOF ¶ 888; Schering FOF Reply ¶ 888). According to Dr. Page, the Bressnick Article concluded that the clinical response to mometasone was decidedly superior to that of hydrocortisone. (T. 985, 1-9; DTX-3 at 25). Dr. Page also testified that the Bressnick Article states that mometasone furoate is very effective clinically and has a low potential for unwanted side effects. (T. 985, 8-9; DTX-3 at 34). Finally, Apotex cites to an expert report drafted in 1986 by one of Schering's physicians. (Apotex FOF ¶ 900). The report states that "because [mometasone furoate] exhibited good topical potency with a low potential for systemic side

effects . . . this suggested that topical mometasone furoate could also have a favorable therapeutic index for the treatment of nasal allergic diseases." (DTX-39 at 2). According to Dr. Page, the approach outlined in this report is consistent with what a skilled pharmacologist would have done in 1990 and consistent with what other companies were doing at the time. (T. 988, 1-14).

In response to Apotex's argument, Schering denies that an ordinary pharmacologist in September 1990 would not have chosen either corticosteroids generally or mometasone furoate specifically as a lead candidate to treat allergic rhinitis. In regard to corticosteroids generally, Schering produced evidence that in September 1990, corticosteroids were only one type of treatment option for allergic rhinitis. At trial Dr. Durham testified that the treatment options for allergic rhinitis in September 1990 included corticosteroids, oral antihistamine tablets, decongestants, and allergic immunotherapy. (T. 1076, 12-25). Dr. Durham further testified that at the same time there was a lot of interest in the development of leukotriene synthesis inhibitors or antagonists for the treatment of allergic reactions. (T. 1078, 22 through T. 1079, 5). In discussing these inhibitors and antagonists, Dr. Durham cited to Victor G. Matassa, et al., *Evolution of a Series of Peptidoleukotriene Antagonists*, 33 Journal of Medicinal Chemistry 1781 (1990) (the "Matassa Article"). (T. 1049, 15-23; *see also* PTX-398). According to Dr. Durham, the Matassa Article reflects that a number of companies were developing antagonists or synthesis inhibitors in 1990 because they were effective in suppressing the symptoms of allergic rhinitis. (T. 1079, 24 through 1080, 11, *see also* PTX-398 at 1).[15] Based on the Matassa Article and on Dr. Durham's testimony,

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[15] For their part, Apotex claims that the Matassa article would not have influenced a skilled pharmacologist since the compounds tested in the Matassa Article were not approved for use in humans in September 1990 and the testing performed in the Matassa paper dealt with guinea pigs. (Apotex FOF ¶¶ 926-29 (citing T. 1095-96)).

Schering argues that since a person of skill in the art could have pursued one of the non-corticosteroid treatment options, Apotex failed to prove that it would have been obvious to select a corticosteroid as the lead compound in a treatment for allergic rhinitis. (Schering COL ¶ 128). Dr. Durham also testified at trial that patients preferred oral treatments to corticosteroids which often required nasal sprays and would sometimes result in local bleeding or crusting of the nose. (T. 1084, 3-10) (T. 1085, 11-17). Based on this testimony, Schering argues that this patient preference would have led a person of ordinary skill towards a non-steroidal once a day tablet as opposed to a corticosteroid spray.

In regard to mometasone furoate, Schering produced evidence that in September of 1990 an ordinary pharmacologist would have been ultimately dissuaded from formulating a nasal spray with mometasone furoate because its metabolism in the liver and metabolites were unknown. In making this argument, Schering relied on both the testimony of Dr. Durham and his review of the Wang Paper. (T. 1086, 4 through T. 1088, 5) (DTX-28). According to Dr. Durham, the metabolism, pharmacokinetics, and toxicokinetics of mometasone furoate had not been evaluated by September 1990. (T. 1086, 12-21 (reviewing the Wang Paper)). Dr. Durham further testified that the lack of knowledge about the metabolism of mometasone furoate would have been a major concern for a PHOSITA identifying a candidate to treat allergic rhinitis. (T. 1087, 2-6). Schering also challenged those conclusions of Dr. Page which were based on the Dominquez and Bressnick Articles. As Schering states in this argument, the Dominquez Article dealt with mometasone furoate cream and the Bressnick Article dealt with mometasone furoate ointment. (Schering FOF ¶¶ 835, 839). Schering further asserts that in September of 1990, if a person developing a treatment for allergic rhinitis actually chose a corticosteroid, the delivery method would have been a nasal spray. (Schering

FOF ¶ 824 (citing T. 1085, 11-16)). Additionally, Schering asserts that the nasal delivery of a corticosteroid would result in a large portion of the drug being swallowed and ultimately passing through the liver. Thus, according to Schering, any conclusions reached by the Dominquez and Bressnick articles with regards to safety or efficacy are inapposite.

(B) Formulating mometasone furoate into an aqueous solution

Apotex claims that there were express directions in the prior art teaching toward formulating mometasone furoate into an aqueous suspension of the monohydrate form. Almost all of Apotex's evidence on this issue was produced at trial through the testimony of Dr. Mitra and his review of the Shapiro patent, the Carless Paper, the Cook Patent, the Wang Patent, and the Hunt Patent. (T. 1028, 2 through T. 1039, 12) (DTX-394) (DTX-105) (DTX-162) (DTX-107). Starting with the Shapiro patent, Dr. Mitra testified that the Shapiro patent is directed toward treating rhinitis. (T. 1028, 5-18). Dr. Mitra also testified that the Shapiro patent specifically disclosed nasal sprays as an example of how to deliver mometasone furoate. (T. 1028, 19-24). Dr. Mitra further testified that a PHOSITA would have prepared a nasal spray of mometasone furoate as a suspension. (T. 1028, 25 through T. 1029-16) (T. 1033, 12 through 1034, 15). Dr. Mitra concluded that any suspension of mometasone furoate prepared according to the Shapiro patent would be substantially similar to the seven aqueous suspensions disclosed in the '353 patent. (T. 1029, 10 through T. 1031, 17).

The second part of Dr. Mitra's testimony dealt with the use of the monohydrate form of mometasone furoate. According to Dr. Mitra, a person of ordinary skill that did not know anything about the likelihood of crystal growth may have attempted to formulate mometasone furoate into an aqueous solution using the anhydrous form. (T. 1032, 9-17). However, as Dr. Mitra explained in trial, in September 1990 it was recognized in the art that pharmaceutical conversion of an anhydrate

of other steroids would lead to particle size growth. (T. 1038, 25 through T. 1039, 7). Thus, in Dr. Mitra's opinion, the logical choice for a PHOSITA was to preemptively avoid the particle size growth problem by formulating with the hydrate or solvate in the first place, maintaining the particle size that is required, and then formulating the steroid into the suspension. (T. 1038, 25 through T. 1039, 12). Importantly, Apotex claims that this process is identical to the process outlined in claims 1 and 11 of the '353 patent. (Apotex FOF ¶ 992).

Dr. Mitra bases his opinion on preempting particle size growth on four prior art articles that would have been available to a PHOSITA in September 1990: the Carless Paper, the Cook Patent, the Wang Patent, and the Hunt Patent. (T. 1035, 7-9). The Carless Paper was published in 1968. (DTX-394). According to Dr. Mitra, the Carless Paper would have taught a PHOSITA that when cortisone acetate, a steroid similar to mometasone furoate, was formulated in an aqueous suspension, it experienced crystal growth and particle size growth. (T. 1035, 18-24). The Cook Patent was published in 1983. (DTX-105). According to Dr. Mitra, the Cook Patent taught a PHOSITA that when belcometasone dipropionate, a steroid similar to mometasone furoate, was formulated with a solvent for an inhalation formulation, it converted to the solvate crystal form and experience crystal size growth. (T. 1036, 9-23). Further discussing the Cook Patent, Dr. Mitra testified that the Cook Patent solved the problem of particle size growth by using the solvated crystal form and then micronizing it to smaller particles. (T. 1036, 20-23). The Wang Patent was also published in 1983. (DTX-162). According to Dr. Mitra, the Wang Patent taught a PHOSITA that a large number of steroids form as monohydrates when in the presence of water. (T. 1037, 25 through 1038, 5). Dr. Mitra further testified that the Wang Patent solved the problem of monohydrate formation by using the monohydrate in the first place, and then micronizing it before adding it to the formulation. (T.

1038, 2-5). The Hunt Patent was issued on September 12, 1989. (DTX-107). According to Dr. Mitra, the Hunt Patent taught a PHOSITA that beclomethasone dipropionate, the same steroid reviewed in the Cook Patent, forms polymorphic crystals in water, which changes the particle size, and further teaches that the steroid crystals have to be micronized. (T. 1038, 16-20). Based on the collective message of these articles, Dr. Mitra concluded that a PHOSITA would be motivated to formulate a nasal suspension with the hydrate form of mometasone furoate. (T. 1038, 25 through T. 1039, 12).

Schering, for its part, denies that there were express directions in the prior art teaching toward formulating mometasone furoate into an aqueous suspension of the monohydrate form. According to Drs. Mitra and Trout, the Shapiro patent discloses neither a formulation for a nasal suspension nor a formulation for a nasal spray. (T. 1057, 19-24) (T. 1240, 25 through T. 1241, 2).

Schering further claims that there significant difference between the four prior art references relied upon by Apotex (i.e., the Carless Paper, the Cook Patent, the Wang Patent, and the Hunt Patent) and the subject matter claimed by the '353 patent. Most of Schering's claims are founded on the testimony of Dr. Trout. At trial, Dr. Trout testified first that a PHOSITA would not have look at the four prior art references to predict the potential existence of additional forms of mometasone furoate or properties of those forms. (T. 1234, 9-13). According to Dr. Trout, "even within a given class, such as a similar class of steroids, one cannot predict either which form would exist, which forms would exist . . . or which forms are stable under a given [set of] conditions. So there was no reason that a [PHOSITA] would consider those references." (T. 1234, 15-20) (*see also* T. 52, 2-18 (testifying that he did not review any patent literature when researching the properties of mometasone furoate to develop the formulation)). Dr. Trout then testified that even if a PHOSITA

had reviewed the four prior art references in combination with the Shapiro patent, it would not have rendered the subject matter of the '353 patent obvious. (T. 1248, 3-7). According to Dr. Trout, none of the four prior art references discuss mometasone furoate. (T. 1248, 10-16). Dr. Trout also testified that none of the four prior art references discuss the monohydrate crystalline form of mometasone furoate. (T. 1248, 9-10). Additionally, Dr. Trout testified that none of the four prior art references discuss aqueous pharmaceutical suspensions. (T. 1236, 25 through T. 1237, 2). Based on these assertions, Schering asserts that the prior art did not teach towards formulating mometasone furoate into an aqueous suspension of the monohydrate form.

(3) The differences between the claimed invention and the prior art

The parties are diametrically opposed on the differences between the claimed invention and the prior art. Apotex claims that "there are no differences between the prior art and the claimed subject matter." (Apotex FOF ¶ 865). Schering claims that "Apotex has not shown, by clear and convincing evidence, that a [PHOSITA] would have been motivated to take anhydrous mometasone furoate and modify it to a previously-unknown and unexpected monohydrate form." (Schering COL ¶ 136). Schering also claims that "Apotex . . . suggest[s] that a [PHOSITA] would have formulated mometasone furoate as a nasal spray, but there is little in [Apotex's] references to support this suggestion, and Apotex has not provided a motivation to combine." (Schering COL ¶ 141).

(4) Objective indicia of non-obviousness

If a patent challenger makes a showing of *prima facie* obviousness, a patentee may rebut the showing with evidence "that the claimed inventions exhibits some superior property or advantage that a [PHOSITA] would have found surprising or unexpected." *Procter & Gamble Co. v. Teva Pharms. USA, Inc.*, 566 F.3d 989, 994 (Fed. Cir. 2009) (internal quotations and citations omitted).

Evidence showing that the invention has an unexpected superior property (sometimes called unexpected results) compared to the prior art can rebut a *prima facie* case of obviousness. *See in re Mayne*, 104 F.3d 1339, 1343-44 (Fed. Cir. 1997); *In re Soni*, 54 F.3d 746, 750 (Fed. Cir. 1995). *Prima facie* obviousness may also be rebutted with objective indicia of nonobviousness (sometimes referred to as "secondary considerations") including the commercial success of the claimed invention. *Procter*, 556 F.3d at 998. Importantly, even though the patentee has the duty of producing such evidence, the burden of persuasion by clear and convincing evidence remains with the patent challenger. *Tech. Licensing Corp. v. Videotek, Inc.*, 545 F.3d 1316, 1329 (Fed. Cir. 2008).

In rebutting Apotex's evidence of *prima facie* obviousness, Schering adduced the testimony of both Dr. Petra Högger[16] and Dr. Stephen Durham as evidence of unexpected results. (T. 1117, 13 through T. 1136, 20) (T. 1065, 11 through T. 1091, 16). At trial, Dr. Högger testified that furoate moiety, a unique structural feature of mometasone furoate, imparted benefits to mometasone furoate which directly supported the increased efficacy and safety of the drug. (T. 1132, 17 through T. 1133, 1) (T. 1135, 14-21). Dr. Högger further testified that in the early 1990s, it was unexpected and not foreseeable that the furoate moiety would impart such benefits to mometasone furoate. (T. 1135, 14-21). On the issue of unexpected results, Dr. Durham testified that mometasone furoate produced unexpected results with regards to safety in children. (T. 1089, 6 through T. 1090, 9 (reviewing PTX-

[16] Dr. Petra Högger is currently a Professor of Clinical Pharmacy, at Julius-Maximilians-University Würzburg, Germany. There Dr. Petra Högger conducts research on pharmacokinetics and pharmacodynamics of pulmonary and intranasally administered drugs, and pulmonary/intranasal delivery of drugs. Dr. Högger also teaches classes relating to clinical pharmacy and therapeutics, clinical chemistry, and pharmacotherapy. At Julius-Maximilians-University, she is a member of Executive Committee of the Academy of Clinical Pharmacy. Dr. Högger also authored over 50 original and review articles in addition to a textbook on clinical pharmacology.

401)). Specifically, Dr. Durham testified that mometasone furoate nasal spray had no effect on the long term growth of children, and that the absence of such growth retardation would not have been expected in September of 1990. (T. 1089, 6-20) (T. 1090, 7-9).

Schering also adduced the testimony of Dr. Christopher Vellturo[17] as evidence of commercial success. (T. 1261, 4 through T. 1288, 3). According to Dr. Vellturo, Nasonex® nasal spray, the product developed from the '353 patent, is a commercial success. (T. 1268, 13-15). Notably, Dr. Vellturo testified that over a span of thirteen years, total net U.S. sales for Nasonex® nasal spray exceeded 5 billion dollars. (T. 1269, 13-15). Dr. Vellturo also testified that the commercial success of Nasonex® is attributable to the formulation using mometasone furoate monohydrate in a nasal suspension. (T. 1268, 16-23) (T. 1281, 7-13). Dr. Vellturo based this opinion on two surveys of physicians that prescribe Nasonex® to treat allergic rhinitis. (T. 1282, 3-8). According to Dr. Vellturo, the main attribute associated with physicians' satisfaction in prescribing Nasonex® was better efficacy. (T. 1285, 3-5). Finally, Dr. Vellturo reviewed the promotional expenditures, the marketing expenditures, and the pricing for Nasonex® and determined that such features were "not inordinately responsible for Nasonex® nasal spray's success over the [thirteen] years in the marketplace." (T. 1286, 3 through T. 1287, 5).

In response, Apotex challenges both of Schering's claims. Regarding Schering's assertion that the invention of the '353 patent produced unexpected results, Apotex refutes Dr. Högger's

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Dr. Christopher A. Vellturo is the founder and president of Quantitative Economic Solutions, LLC, an economic consulting firm. Dr. Vellturo is also employed by Boston University, in Boston, Massachusetts, where he teaches graduate-level economics. Dr. Vellturo received a Doctor of Philosophy degree (Ph.D.) in Economics from the Massachusetts Institute of Technology in Cambridge, Massachusetts in 1989. My fields of specialization include industrial organization and econometrics.

testimony. (Apotex FOF ¶¶ 1001-14, 1031-40). On cross examination, Dr. Högger admitted that she never gave the opinion in her expert report that the unexpected results of mometasone furoate were due to the monohydrate form of mometasone furoate. (T. 1145, 22-25). Dr. Högger also admitted at trial that she never discussed the monohydrate form of mometasone furoate anywhere in her expert report, nor had she performed any studies to determine that the unexpected results discussed in her expert report were due to the monohydrate form of mometasone furoate. (T. 1147, 14-19). Based on this testimony, Apotex asserts that Schering failed to prove that the unexpected results alleged by Dr. Högger have any nexus to the monohydrate form of mometasone furoate, as opposed to mometasone furoate itself which was previously patented by the Shapiro patent. (Apotex COL ¶ 256). Regarding Schering's evidence of commercial success, Apotex challenges the assertions of Schering's expert with their own expert on commercial success, Mr. Harry Charles Boghigian.[18] (T. 1313, 23 through T. 1337, 19). Mr. Boghigian testified that the market performance of Nasonex® had nothing to do with the '353 patent. (T. 1320, 3-14). Rather, Mr. Boghigian asserts that the performance of Nasonex® is entirely due to marketing and promotion. (T. 1319, 16-19).

(5) Analysis

Based on the foregoing, the Court determines that the '353 patent would not have been obvious to a PHOSITA in September of 1990. First, the Court agrees with Dr. Trout that the level of ordinary skill in the art in September of 1990 would not require a PHOSITA to have specific experience in the development of aqueous nasal suspensions. When asked if a person of skill in the art related to the '353 patent would have specific experience in the development of nasal suspension,

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[18] Mr. Boghigian is a pharmaceutical executive with over forty years of domestic and international experience in the commercialization and marketing of pharmaceutical products.

Dr. Trout testified that it would not "[b]ecause the '353 patent focuses on specific composition of matter, mometasone furoate monohydrate . . . ." (T. 1229, 1-8). Additionally, Dr. Mitra testified that the development process described in the '353 patent is "a multidisciplinary process and requires collaborative teamwork and is done in the industry routinely from various groups with various expertise." (T. 1021, 16-20). Based on this testimony, the Court finds that the broader definition of a PHOSITA is appropriate.

Second, the Court finds that Apotex failed to meet their burden to prove that a PHOSITA would have been motivated to develop a nasal spray using mometasone furoate. Dr. Durham testified convincingly that in September of 1990, the fact that the metabolism of mometasone furoate in the liver was unknown would have been a "major concern" about the systemic effects of nasal delivery of the drug. (T. 1087, 2-15). Dr. Durham went on to testify that "there were questions regarding [the] safety of the mometasone at the time . . . [e]ven though it [had] been used in the skin effectively . . . ." (T. 1088, 3-8). Conversely, Dr. Page's discussion of mometasone furoate's safety dealt with creams that did not pass through the liver. (T. 980, 6 through T. 981, 1) (T. 981, 7-12). Dr. Durham's testimony thus undermines the assertion that it would have been obvious to a PHOSITA to develop a treatment for allergic rhinitis using mometasone furoate, at least to the extent the treatment was developed as a nasal spray. Additionally, in support of the position that it would have been obvious to develop a treatment for allergic rhinitis into a nasal spray, Apotex adduced the testimony of Dr. Mitra. (T. 1016, 4 through T. 1040, 20). After reviewing the prior art, Dr. Mitra testified that the "collective message" of the prior art "is if you're taking the steroids, including mometasone, . . . they all in water or in [the] presence of any solvent, will forma hydrate or a solvate, and then change particle size and will grow. [T]he message is that you need to formulate . . . by

changing the particle size back to what you want, and then formulate the suspension." (T. 1038, 25 through T. 1039, 12). This conclusion was directly contradicted by Dr. Trout. According to Dr. Trout, "even within a given class [of steroids], one cannot predict either which form would exist, which forms would exist . . . or which forms are stable." (T. 1234, 15-20). Dr. Trout went on to testify that "for several decades people have tried to develop thermodynamic theories and other theories in order to make these predictions, but unfortunately even today the state of the art is such that we don't have accurate technologies to do that." (T. 1231, 21-25). The Court found Dr. Trout both truthful and persuasive and gives weight to his testimony. Comparatively, Dr. Mitra analysis and conclusion appeared hamstrung by the materials and direction provided to Dr. Mitra by Apotex. (T. 1054, 14 through T. 1055, 2).

Finally, since the Court determines that Apotex failed to make a *prima facie* case for obvious, there is no need to review the objective indicia of non-obviousness. *See Yamanouchi Pharm. Co. v. Danbury Pharmacal, Inc.*, 231 F.3d 1339, 1345 (Fed. Cir. 2000) ("Because [Defendant] did not show even a *prima facie* case for obviousness, this court has considered, but need not separately address, the strong objective evidence of non obviousness.").

CONCLUSION

For the reasons stated above, Schering's complaint for infringement is dismissed because Schering failed to present credible evidence sufficient to meet its burden of proof by a preponderance of the evidence standard. Additionally, Apotex's counterclaim for invalidity is dismissed because Apotex failed to present credible evidence sufficient to meet its burden of proof by a preponderance of the evidence standard. An appropriate form of order will follow.

s/Peter G. Sheridan
PETER G. SHERIDAN, U.S.D.J.

June 15, 2012